

DECLARATION FOR NON-PROVISIONAL PATENT APPLICATION*

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below at 201 et seq. beneath my name.

I believe I am the original, first and sole inventor if only one name is listed at 201 below, or an original, first and joint inventor if plural names are listed at 201 et seq. below, of the subject matter which is claimed and for which a patent is sought on the invention entitled

ANTI-RESORPTIVE BONE CEMENTS AND ALLOGENEIC, AUTOGRAFIC, AND XENOGRAFIC BONE GRAFTS

and for which a patent application:

- ☐ is attached hereto and includes amendment(s) filed on *(if applicable)*
☐ was filed in the United States on as Application No. *(for declaration not accompanying application)*
 with amendment(s) filed on *(if applicable)*
☒ was filed as PCT international Application No. PCT/US00/03285 on February 9, 2000.

I hereby state that I have reviewed and understand the contents of the above identified application, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

EARLIEST FOREIGN APPLICATION(S), IF ANY, FILED PRIOR TO THE FILING DATE OF THE APPLICATION			
APPLICATION NUMBER	COUNTRY	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
			YES <input type="checkbox"/> NO <input type="checkbox"/>
			YES <input type="checkbox"/> NO <input type="checkbox"/>
			YES <input type="checkbox"/> NO <input type="checkbox"/>

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below.

PROVISIONAL APPLICATION NUMBER	FILING DATE
60/119,260	February 9, 1999

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information known to me which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

NON-PROVISIONAL APPLICATION SERIAL NO.	FILING DATE	STATUS		
		PATENTED	PENDING	ABANDONED

* for use only when the application is assigned to a company, partnership or other organization.

ANTI-RESORPTIVE BONE CEMENTS AND ALLOGENEIC,
AUTOGRAFIC, AND XENOGRAFIC BONE GRAFTS

5 This application claims the benefit of United States Provisional application serial No. 60/119,260, filed February 9, 1999, incorporated by reference herein in its entirety.

1. **FIELD OF THE INVENTION**

10 The present invention concerns an anti-resorptive bone cement. The present invention also relates to an anti-resorptive allogeneic bone graft, an anti-resorptive autografic bone graft, and an anti-resorptive xenografic bone graft. More particularly, the present invention concerns a bone cement comprising an anti-resorptive agent, an allogeneic bone graft comprising an anti-resorptive agent, an autografic bone graft comprising an anti-resorptive agent, and a xenografic bone graft comprising an anti-
15 resorptive agent, wherein the anti-resorptive agent is selected from the group consisting of bisphosphonates and their pharmaceutically acceptable salts or esters; salts of a Group IIIA elements; cholesterol lowering agents; bisphosphonate-chemotherapeutic agent conjugates; estrogen-bisphosphonate conjugates; and proteinaceous or hormonal anti-resorptive agents, such as estrogens, prostaglandins, and cytokines.

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2. **BACKGROUND OF THE INVENTION**

Bone Loss and Orthopaedic Implants

Progressive bone loss and pathologic fracture are major sources of skeletal pain and prosthetic failure in cancer patients.

25 Bone cement is used to grout most orthopaedic joint replacements. The greatest problem plaguing the durability of the implant fixation is aseptic loosening. This is induced by particulate debris shed from the implant and mediated by osteoclastic bone resorbing cells.

Thus, post-surgical bone loss associated with the use of bone cement, such as
30 acrylic bone cement, is frequently responsible for the loosening of prosthetic implants. These osteolytic processes are associated with osteoclast activity.

Cemented orthopaedic implants undergo time dependent aseptic loosening (Martell, J.M., Berdia, S., "Determination of polyethylene wear in total hip replacement with use of the digital radiographs", *J. Bone Joint Surg. Am.*, 79:11, 1635-1642 (1997); Madey, S.M.,
35 Callaghan, J.J., Olejniczak, J.P., Goetz, D.D., Johnston, R.C., "Charnley total hip arthroplasty with use of improved techniques of cementing. The results after a minimum